K081895

510(k) Summary

JAN - 8 2009

Submitter information

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Device Trade or Proprietary Names: ADVIA® Chemistry Hemoglobin A1c Assay
ADVIA® Chemistry A1c Calibrators

Device Common/Usual Name or Classification Name: Glycosylated Hemoglobin Assay Calibrators

Classification Number/Class: LCP / Class II
JIX / Class II

This 510(k) summary of safety and effectiveness is being submitted in accordance with the requirements of 21 CFR 807.92.

The assigned 510(k) number is: _k081895_

Assay Predicate Device:

	Predicate Device
Device Name	G7 Automated HPLC Analyzer – HbA1c Variant Analysis Mode
Common name	Glycosylated Hemoglobin Test
510(k) Number	k011434
Manufacturer	Tosoh Medics, Inc.

Calibrator Predicate Device:

	Predicate Device
Device Name	VITROS Chemistry Products Calibrator Kit 18
Common name	Calibrator
510(k) Number	k041764
Manufacturer	Ortho-Clinical Diagnostics

Device Description:

The concentration of A1c and the concentration of total hemoglobin are measured and the ratio is reported (either as % or mmol/mol).

There are two different sample pretreatment methods available on the ADVIA Chemistry System. The first method is an Automated Pretreatment that uses 4 reagents: A1c Denaturant Reagent, Total Hemoglobin Reagent (tHb_2), A1c Agglutinator Reagent (R1) and A1c Antibody Reagent (R2). In this Automated Pretreatment step, the whole blood sample is mixed with the A1c Denaturant Reagent. The red blood cells are lysed and the hemoglobin chains are hydrolyzed by the protease present in the reagent.

The second method is a Manual Pretreatment that uses the same reagents as the first method except that the A1c Denaturant Reagent is replaced with the Hemoglobin Denaturant Reagent. For this method, there is an off-line pretreatment that is followed by a 10 minute incubation.

For the measurement of total hemoglobin, the Total Hemoglobin Reagent is used. The method is based on the conversion of all hemoglobin derivatives into alkaline hematin in an alkaline solution of a nonionic detergent

A latex agglutination inhibition method is used for the measurement of specific A1c. The A1c present in the sample competes with the agglutinator (synthetic latex containing multiple copies of the immunoreactive portion of A1c) for the anti-A1c antibody; thereby reducing the rate of agglutination. A concentration curve is obtained by monitoring the change in scattered light as a change of absorbance. The actual change in absorbance is inversely proportional to the concentration of A1c in the sample. The HbA1cN NGSP result (%) or the HbA1cI IFCC result (mmol/mol) is calculated using the A1c and total hemoglobin values.

The ADVIA® Chemistry A1c Calibrators are used to calibrate the methods. The calibrators consist of four (4) levels of lyophilized whole blood containing varying concentrations of HbA1c and total hemoglobin. There is a single level calibration for total hemoglobin (Cal 1) and a multi-level calibration (six levels) for A1c. Four calibrator levels (designated Cal 1 – 4) are provided in a single kit and each level is 0.5 g/vial. The other two levels consist of Saline (Cal 0) and Cal 5 (prepared by the system from Cal 4 using 1.4 times the volume used for Cal 4).

The target value of each calibrator (calibration) level is:

- Calibration Level 1 (Cal 0): 0.00 µmol/L A1c, 0.0 g/dL Total Hemoglobin
- Calibration Level 2 (Cal 1): 2.30 µmol/L A1c, 11.0 g/dL Total Hemoglobin
- Calibration Level 3 (Cal 2): 3.65 µmol/L A1c
- Calibration Level 4 (Cal 3): 5.15 µmol/L A1c
- Calibration Level 5 (Cal 4): 6.80 µmol/L A1c
- Calibration Level 6 (Cal 5): 8.20 µmol/L A1c

Storage is at 2 - 8°C.

CAUTION! POTENTIAL BIOHAZARD: Contains human source material. While each human serum or plasma donor unit used in the manufacture of this product was tested by FDA-approved methods and found nonreactive for hepatitis B surface antigen (HBsAg), antibody to hepatitis C (HCV), and antibody to HIV-1/2, all products manufactured using human source material should be handled as potentially infectious. Because no test method can offer complete assurance that hepatitis B or C viruses, HIV, or other infectious agents are absent, these products should be handled according to established good laboratory practices.

Statement of Intended Use:

The ADVIA® Chemistry Hemoglobin A1c method is for *in vitro* diagnostic use in the quantitative determination of Hemoglobin A1c, a diabetes marker, in whole blood on the ADVIA Chemistry systems. Such measurements are used for monitoring the long-term glycemic control of persons with diabetes. The A1c and total hemoglobin (tHb) values generated as part of the HbA1cN and HbA1cI methods are intended for use in the calculation of the A1c / total hemoglobin ratio, and must not be used individually for diagnostic purposes.

*Note: HbA1cN reports HbA1c in % and HbA1cI reports HbA1c in mmol/mol

The ADVIA® Chemistry A1c Calibrators are for *in vitro* diagnostic use in the calibration of the A1c and total hemoglobin methods (Automated and Manual Pretreatment) on the ADVIA Chemistry Systems.

Comparisons to the Predicate Device:

Method Similarities

	ADVIA Chemistry Hemoglobin A1c ***(new device)***	Tosoh G7 Automated HPLC Analyzer – HbA1c Variant Analysis Mode ***(predicate device)***
Intended Use	For *in vitro* diagnostic use for the measurement of hemoglobin A1c	For *in vitro* diagnostic use for the measurement of hemoglobin A1c
Specimen Type	Human Whole Blood (EDTA and Lithium Heparin)	Human Whole Blood
Standardization	Traceable to NGSP*** Traceable to IFCC by Master Equation	Traceable to NGSP***

Method Differences

	ADVIA Chemistry Hemoglobin A1c *(new device)*	Tosoh G7 Automated HPLC Analyzer – HbA1c Variant Analysis Mode *(predicate device)*
Assay Principle	For Hemoglobin: Conversion of all hemoglobin derivatives into alkaline hematin For HbA1c: Latex agglutination inhibition	High Performance Liquid Chromatography (non-porous ion exchange)
Determination / Calculation of results	Ratio of HbA1c/ Total Hemoglobin	Measurement of HbA1c as a percentage of total hemoglobin
Calibration	Multipoint calibration (6 levels) for Hemoglobin A1c Single point calibration for Total Hemoglobin	2 point Calibration (high and low)
Analytical Range	2.9 – 15.4%	4.2 – 20.8%

Calibrator Similarities

	ADVIA Chemistry A1c Calibrators *(new device)*	VITROS Chemistry Products Calibrator Kit 18 *(predicate device)*
Intended Use	For *in vitro* diagnostic use in the calibration of the A1c and total hemoglobin methods (Automated and Manual Pretreatment) on the ADVIA Chemistry Systems	For *in vitro* diagnostic use only. VITROS Chemistry Products Calibrator Kit 18 is used in conjunction with VITROS Chemistry Products FS Calibrator 1 to calibrate VITROS 5, 1 FS Chemistry Systems for the calculation of percent glycated hemoglobin (%A1c).
Calibrator Levels	4 levels provided	4 levels provided
Matrix / Ingredients	Processed human whole blood	Hemolysate derived from human and ovine blood, surfactants, stabilizer, and preservatives
Form	Lyophilized	Lyophilized
Storage	2 – 8°C	2 – 8°C
Shelf Life Stability	stable until the expiration date	stable until the expiration date
Reconstituted Vial / Use Stability	7 days stored at 2 – 8°C	2 days stored at 2 – 8°C

Calibrator Differences

	ADVIA Chemistry A1c Calibrators *(new device)*	VITROS Chemistry Products Calibrator Kit 18 *(predicate device)*
Instructions for Use (Preparation)	Reconstitute with DI water before use	Reconstitute with diluent before use

Performance:

Substantial equivalence was demonstrated by testing several performance characteristics including imprecision, method comparison, interfering substances, matrix equivalency, and analytical range. The following tables summarize the precision (total), interfering substances, analytical range, and method comparison results.

All of the evaluation studies gave acceptable results compared to the Predicate Device. These studies support that the ADVIA Chemistry Hemoglobin A1c assay (with the ADVIA Chemistry A1c Calibrators) is substantially equivalent to the Tosoh G7 HPLC Hemoglobin A1c method that is currently marketed.

Imprecision

ADVIA Chemistry Hemoglobin A1c		**ADVIA Chemistry Hemoglobin A1c**		**Tosoh G7 HPLC HbA1c**	
ADVIA 1800 - Automated		**ADVIA 1800 - Manual**			
Level HbA1c (%)	Total CV (%)	Level HbA1c (%)	Total CV (%)	Level HbA1c (%)	Total CV (%)
5.5	1.9	5.0	1.9	5.8	1.12
9.6	1.3	8.8	1.4	10.9	0.71

Correlation

(y = ADVIA Chemistry Hemoglobin A1c, x = comparison method/system)

System (y)	N	Regression Equation	r	Sy.x	Sample Range (%)
ADVIA 1800 Automated – Least Squares	80	y = 0.98x + 0.17	0.997	0.17	4.40 – 12.60
ADVIA 1800 Automated – Passing Bablok / Pearson's	80	y = 1.00x + 0.06	1.00	--	4.40 – 12.60
ADVIA 1800 Manual – Least Squares	80	y = 0.95x + 0.26	0.995	0.19	4.40 – 12.60
ADVIA 1800 Manual – Passing Bablok / Pearson's	80	y = 0.97x + 0.10	1.00	--	4.40 – 12.60

x = NGSP Reference Method (Tosoh G7), y = ADVIA Chemistry System

Interfering Substances (ADVIA Chemistry Hemoglobin A1c on ADVIA 1800)

Automated Sample Pretreatment

Interfering Substance	Interferent Conc. (mg/dL)	HbA1c conc. (%)	Effect (% change)
Triglycerides (Intralipid)	500 mg/dL	5.2	- 7.8
Bilirubin, free	60 mg/dL	5.3	- 1.9
Bilirubin, conjugated	60 mg/dL	5.2	- 3.8

Manual Sample Pretreatment

Interfering Substance	Interferent Conc. (mg/dL)	HbA1c conc. (%)	Effect (% change)
Triglycerides (Intralipid)	500 mg/dL	5.2	- 7.7
Bilirubin, free	60 mg/dL	5.1	- 2.0
Bilirubin, conjugated	60 mg/dL	5.1	- 5.9
Rheumatoid Factor	1100 IU/mL	4.8	0

Analytical Range

Platform	Analytical Range
All ADVIA Chemistry	~~1.7 – Calibrator Level 6 (12.3 – 18.6%)~~ 2.9% – 15.4 %

Conclusions:

The ADVIA Chemistry Hemoglobin A1c method and Calibrators are substantially equivalent to other products in commercial distribution intended for similar use. Most notably, it is substantially equivalent to the currently marketed Tosoh G7 Automated HPLC Analyzer– HbA1c Variant Analysis Mode. The Tosoh G7 Automated HPLC Analyzer is certified by the National Glycohemoglobin Standardization Program (NGSP) and it is used as a reference method for establishing traceable results of other methods to the Diabetes Control and Complications Trial (DCCT).

The ADVIA Chemistry A1c Calibrators are substantially equivalent to the Predicate Device VITROS Chemistry Products Calibrator Kit 18.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
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Rockville MD 20850

Siemens Healthcare Diagnostic
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Tarrytown, NY 10591

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Re: k081895
Trade/Device Name: ADVIA Chemistry Hemoglobin A1c Assay, ADVIA Chemistry A1c Calibrators
Regulation Number: 21 CFR 864.7470
Regulation Name: Glycosylate hemoglobin assay.
Regulatory Class: Class II
Product Code: LCP, JIX
Dated: November 18, 2008
Received: November 19, 2008

Dear Dr. Liu:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific information about the application of labeling requirements to your device, or questions on the promotion and advertising of your device, please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at (301) 594-3084. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its Internet address http://www.fda.gov/cdrh/dsma/dsmamain.html.

Sincerely yours,

Courtney C. Harper, Ph.D.
Acting Director
Division of Chemistry and Toxicology
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and
Radiological Health

Enclosure

Indication for Use

510(k) Number (if known): k081895

Device Name(s):

ADVIA® Chemistry Hemoglobin A1c
ADVIA® Chemistry A1c Calibrators

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Prescription Use _X_ (21 CFR Part 801 Subpart D) And/Or Over the Counter Use ____. (21 CFR Part 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE; CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD)

Carol C Benson

Division Sign-Off
Office of In Vitro Diagnostic Device
Evaluation and Safety

510(k) K081895